THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION: Barros et al.	§	
	§	
	§	
Serial No.: 10/528,500	§	**Group Art Unit: 1655**
	§	
Filed: March 18, 2005	§	**Examiner: Tate, Christopher R.**
	§	
For: Gel Composition Comprising 4-Nerolidylcatechol and Uses Thereof	§	

Mail Stop Appeals
Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

ATTENTION: Board of Patent Appeals
and Interferences

APPELLANT'S BRIEF (37 C.F.R. § 41.37)

This brief is in furtherance of the Notice of Appeal, filed in this case on July 8, 2009.

Please charge a fee under § 41.20(b)(2) in the amount of $540.00 for the filing of this Appeal Brief. No other fees are believed to be due. If, however, any fees are required, I authorize the Commissioner to charge these fees to Carstens & Cahoon LLP, Deposit Account No. 50-0392.

I. REAL PARTIES IN INTEREST (37 C.F.R. 41.37(c)(1)(i))

The real parties in interest in this appeal are Universidade de Sao Palo and Fundacao de Amparo a Pesquisa de Estado de Sao Paulo.

II. RELATED APPEALS AND INTERFERENCES (37 C.F.R. 41.37(c)(1)(ii))

With respect to other appeals or interferences that will directly affect, or be directly affected by, or have a bearing on the Board's decision in the pending appeal, there are no such appeals or interferences.

III. STATUS OF CLAIMS (37 C.F.R. 41.37(c)(1)(iii))

A. **TOTAL NUMBER OF CLAIMS IN APPLICATION**

Claims in the application are: 24, 27, 28.

B. **STATUS OF ALL THE CLAIMS IN APPLICATION**

1. Claims pending: 24, 27, 28.
2. Claims previously cancelled: 1-23, 25-26, 29-30.
3. Claims withdrawn: None
4. Claims rejected: 24, 27, 28
5. Claims allowed: None.
6. Claims cancelled in accompanying amendment: None.

C. **CLAIMS ON APPEAL**

The claims on appeal are: 24, 27, 28.

IV. STATUS OF AMENDMENTS (37 C.F.R. 41.37(c)(1)(iv))

No amendments were filed after final rejection.

V. SUMMARY OF THE CLAIMED SUBJECT MATTER (37 C.F.R. 41.37(c)(1)(v))

The claimed invention is related to a composition for topical use and a method of use for said composition. Claim 24 is directed towards a gel composition for topical use (p. 11, lines 1-12), said gel comprising:

a) carboxymethylcellulose from 0.01 to 2.0% (p. 11, line 7);

b) propylene glycol from 5.0 to 20.0% (p. 11, line 8);

c) methylparaben from 0.1 to 1.0% (p. 11, line 9); and

d) 4-nerolidylcatechol from 0.005 to 20.0% (p. 11, lines 10-12).

Claim 28 is directed towards a method of treating skin photodamage, cutaneous aging and/or skin cancer by topically administering a gel composition (p. 11, lines 1-12; p. 13, lines 13-23), said gel comprising:

a) carboxymethylcellulose from 0.01 to 2.0% (p. 11, line 7);

b) propylene glycol from 5.0 to 20.0% (p. 11, line 8);

c) methylparaben from 0.1 to 1.0% (p. 11, line 9); and

d) 4-nerolidylcatechol from 0.005 to 20.0% (p. 11, lines 10-12).

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL (37 C.F.R. 41.37(c)(1)(vi))

1. Claims 24, 27 and 28 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement.

2. Claims 24, 27 and 28 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Ropke et al. (Free Radical Biol. Med., Vol 33, Issue 2, Abstract #527, 15 July 2002) and Ropke et al. (Annals of the 14th National Cosmetology Congress of the Brazilian Cosmetology Assoc, 2000) in view of Wheeler et al. (US 6,165,479) and, if necessary, the admitted state of the art.

3. Claims 24, 27, and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Uchiyama et al. (JP 2001122763) in view of Barros et al. (Ciencia e Cultura, 1996) and Desmarchelier et al. (Planta Med, 1997), and further in view of Wheeler et al. (US 6,165,479) and, if necessary, the admitted state of the art.

VII. ARGUMENTS (37 C.F.R. 41.37(c)(1)(vii))

REJECTIONS UNDER 35 U.S.C. 112(b)

Group I: Claims 24, 27 and 28

Claims 24, 27 and 28 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement.

Ranges in a claim can be narrower than those disclosed in specification. In *Ralston Purina Co. v. Far-Mar-Co.*, 772 F.2d 1570, 1575 (Fed. Cir. 1985), the Federal Circuit expressly rejected the notion "that ranges found in the applicant's claim language must correspond exactly to ranges disclosed in the parent." This is because neither the Patent Act nor the case law requires such detailed disclosure. *See In re Hayes Microcomputer*

Prods., Inc., 982 F.2d 1527, 1533 (Fed. Cir. 1992) ("[The applicant] does not have to describe exactly the subject matter claimed."); *Vas-Cath v. Mahurkar*, 935 F.2d 1555, 1566 (Fed. Cir. 1991) ("ranges found in applicant's claims need not correspond exactly to those disclosed in [the specification]; issue is whether one skilled in the art could derive the claimed ranges from the [] disclosure."). Rather, the Patent Act and this court's case law require only sufficient description to show one of skill in the refining art that the inventor possessed the claimed invention at the time of filing. *Union Oil Co. v. Atlantic Richfield Co.*, 208 F.3d 989, 1001 (Fed. Cir. 2000). To satisfy the written description requirement, the claimed invention need not be expressed *ipsis verbis* in the original specification. *In re Wertheim*, 541 F.2d 257, 262, 190 U.S.P.Q. 90, 96 (C.C.P.A. 1976). In *In re Wertheim*, the CCPA found that a claimed range of 35% to 60% based upon a written description disclosing a range of 25% to 60% having did meet the description requirement. *See also* MPEP 2163.05 III. Applicants' claimed ranges are within the ranges disclosed in the specification, like the range in *In re Wertheim*.

Additionally, a gel composition for the treatment and/or prevention of photodamage to skin, cutaneous ageing and/or skin cancer, on the basis of *Pothomorphe umbellata* extract comprising a standardized extract of *Pothomorphe umbellata*, which contains a range from 0.005 to 20.0% of 4-nerolidylcatechol in the composition, as claimed in claim 24, is fully supported by specification of the present application (paragraph 34).

Likewise, the claimed gel composition, "comprising carboxymethylcellulose 0.01-10. %; propyleneglycol 0.001-50.0%; methylparaben 0001-3.0% and *Pothomorphe umbellata* standardized extract, so that the formulation comprises from 4-

nerolidylcatechol 0.005 to 20.0%" claimed in claims 24 and 28 is also fully supported by the specification. The preparation of the composition itself is not specifically described in the specification; however, it is mentioned that the composition of this invention can be made through any known methods in the pharmacy art. Therefore, the applicant is claiming only a gel composition and a method of treating comprising topically administration with said gel composition, and not the process of preparation of gel composition.

Additionally, the specification mentions that a possible source for 4-nerolidylcatechol is a *Pothomorphe umbellata* rot extract. Although it is not specifically mentioned in the specification, someone skilled in the art would know that 4-nerolidylcatechol could be obtained by any other means (other plants extracts, organic synthesis, etc).

Therefore, claims 24, 27 and 28 meet the written description requirement of 35 U.S.C. § 112. Consequently, Applicants respectfully request that the Board overturn the Examiner's rejections as to claims 24, 27 and 28.

REJECTIONS UNDER 35 U.S.C. 103

The Examiner has rejected claims 24, 27 and 28 under 35 U.S.C. § 103(a) as being unpatentable over Ropke et al. (Free Radical Biol. Med., Vol 33, Issue 2, Abstract #527, 15 July 2002) and Ropke et al. (Annals of the 14th National Cosmetology Congress of the Brazilian Cosmetology Assoc, 2000) in view of Wheeler et al. (US 6,165,479) and, if necessary, the admitted state of the art. The Examiner has further rejected claims 24, 27, and 28 under 35 U.S.C. 103(a) as being unpatentable over Uchiyama et al. (JP

2001122763) in view of Barros et al. (Ciencia e Cultura, 1996) and Desmarchelier et al. (Planta Med, 1997), and further in view of Wheeler et al. (US 6,165,479) and, if necessary, the admitted state of the art.

Applicants emphasize that on page 7, line 16 of the specification it is disclosed that although the antioxidant activity of *Pariparoba* was known, it is not obvious to imagine which specific gel formulation serves as a vehicle for this drug in order to obtain a therapeutically effective gel composition. Furthermore, there are not specific studies about the performance of active principle of this plant in the oxidative stress caused by ultraviolet radiation. Figure 3 shows the effectiveness of the proposed vehicle showing that 4-nerolidylcatechol is present on (into) the skin. In the present application, it was demonstrated for the first time the activity *in vivo* of the extract in mice chronically exposed to ultraviolet radiation.

Applicants assert that the inventive activity of present application is focused on developing a formulation containing extract of the plant and that it contains the 4-nerolidylcatechol so that the final concentration of this compound in the formulation is between 0.005 to 20% to produce photoprotector effect *in vivo*.

Moreover, examples 1 and 2 specifically demonstrate the effect of the topical application of a gel containing 0.1% of 4-nerolidylcatechol. Example 1 teaches that a topical application of a gel containing 0.1% of 4-nerolidylcatechol preserves the levels of tocopherol in the skin of irradiated mice, thus protecting it against degradation from UV radiation. Example 2 teaches that a topical application of a gel composition containing 4-nerolidylcatechol in the concentration of 0.1% reduces photoaging in the skin of UV irradiated mice.

That is to say, it would not be obvious as to what specific gel formulation to use in order to obtain a therapeutically effective gel composition. First of all, it would not be obvious as to what specific combination of common skin gel components to use in such gel composition comprising 4-nerolidylcatechol. Secondly, it would surely not be obvious as to what quantities of each of the components should be used in said gel composition.

Additionally, in order to exhibit photoprotective properties, a given antioxidant must be photostable after UV exposure. Previous studies of *Pothomorphe umbellata* extracts have not employed UV radiation; thus, it was not obvious at time of claimed invention as to which specific formulation containing an extract of *Pothomorphe umbellata* and/or 4-nerolidylcatechol would be photostable. The results shown in Example 2 demonstrate that the claimed composition is capable of protecting the skin against UV radiation after UV exposure and therefore exhibits the desired photostability properties (FIG. 5).

In fact, it must be noted that it is the specific combination of the components of the claimed gel composition that grants its therapeutic properties. It is well known in the art that a given antioxidant must permeate the *stratum corneum* so that the active principle reaches the viable skin to exert its antioxidant activity. This permeation depends not only on the structure of the antioxidant compound itself but also on the specific formulation used and the interaction between the compound itself and the formulation used with the skin. Example 1 of the specification demonstrates that the claimed composition indeed has the ability to deliver 4-nerolidylcatechol into the skin (FIG. 3) and it can therefore be used topically for therapeutic purposes.

The advantage of the present invention is that the specific combination and amounts of the components of the claimed gel composition provides its properties, i.e., absorption by skin, protection against UV and antioxidant potential activities.

Based on the above arguments, it would not have been obvious to imagine an extract of *Pothomorphe umbellata* in a gel formulation with the specified components. Furthermore, it would not be obvious that such gel composition with *Pothomorphe umbellata* extract has photoprotective activity. Consequently, Applicants respectfully request that the Board overturn the Examiner's rejections as to claims 24, 27 and 28.

With respect to the rejection in view of the two Ropke et al. and Wheeler et al. references, Applicants believe that the two cited Ropke et al. references do not show the features as asserted by the Office Action. On page 3 of the Office Action, the Examiner considers the publications of Ropke et al. (2002) and Ropke et al. (2000) to disclose the topical use of a gel. In the Ropke et al (2002) reference, although the summary mentioned the use of gel, the components of said gel were not specified. Furthermore, as stated in the Response to Final Office Action filed on February 5, 2008, the Ropke et al. (2002) reference should not be considered prior art by the Examiner, since it was published by the inventors within the grace period of the present application (Ropke et al. (2002) was published by the inventors themselves, two months prior to the filing of the Brazilian priority application (PI0204130-8) which was filed on September 18th, 2002).

Also, the Ropke et al. (2000) reference does not disclose a gel. There are four categories of semi-solid preparations disclosed: ointments, creams, gels or paste. Gels are semi-solid system consisting of suspensions of small inorganic particles or large organic molecules interpenetrate by a liquid, as is the formulation of the present application,

while ointments are preparations for topical application, consisting of a single base, which may be dispersed solids or liquids, for example, Diadermine. Therefore, Applicants respectfully submit that Examiner made a conceptual error in such assumption. As known by a person with ordinary skill in the art, gels and Diadermine compositions are completely different and the incorporation of an active ingredient in these compounds results in completely different therapeutics effects.

A prima facie case of obviousness is established when the teachings of the prior art itself suggest the claimed subject matter to a person of ordinary skill in the art. *In re Bell*, 991 F.2d 781, 783, 26 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1993). On page 4, paragraph 2 of the Office Action, the Examiner states that Wheeler et al. teaches that carboxymethylcellulose, propylene glycol, and methylparaben are well known conventional ingredients within skin therapeutic compositions. However, Applicants assert that the present invention is not limited to a simple addition of an antioxidant to the composition, but a composition that presents photoprotective activity *in vivo*, wherein lies the non-obviousness of the invention.

Also, on page 4, paragraph 3, Applicants disclose that the present invention is not based on antioxidant activity, but on photoprotective activity (photodamage). It is not possible to say that any substance that presents antioxidant activity is a photoprotector. Therefore, it would not be obvious to one of ordinary skill in the art to deduce this property. On page 7, line 16 of the specification of the present application, it was mentioned that although the antioxidant activity have been known (prior art), the absorption on skin was fundamental to the effect *in vivo*, which shows the protection of the skin against ultraviolet radiation. Consequently, the teachings of the prior art do not

suggest the claimed subject matter to a person of ordinary skill in the art. In view of this, Applicants respectfully request that the Board overturn the Examiner's rejections as to claims 24, 27 and 28.

With respect to the Examiner's rejection based on Uchiyama et al., Barros et al., Desmarchelier et al., and Wheeler et al., a prima facie case of obviousness is established when the teachings of the prior art itself suggest the claimed subject matter to a person of ordinary skill in the art. *In re Bell*, 991 F.2d 781, 783, 26 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1993). Uchiyama et al. refers to formulations with antioxidant activity and does not indicate the formulations which are in the form of gel. Barros et al. (1996) and Desmarchelier et al. teaches only a composition comprising an antioxidant activity. None of the references, including Uchimyama et al., expressly teach providing the skin with therapeutic *Pothomorphe umbellata* extract within a skin gel composition including photoprotective activity. The Wheeler et al. reference does not show the photoprotective activity of these formulations containing carboxymethylcellulose, propylene glycol, and methylparaben. Consequently, the teachings of the prior art do not suggest the claimed subject matter to a person of ordinary skill in the art.

Moreover, the therapeutic gel composition of the present application is not merely a matter of common selection and routine optimization which is well within the experience of a person with ordinary skill in the art. The composition of the present invention is a formulation in gel form containing the extract which creates the effects claimed in claim 28. Therefore, it is not obvious that mixing the *Pothomorphe umbellata* extract will induce the photoprotective activity.

All references cited as prior art refer only to the antioxidant activity and Wheeler et al. refers only to compositions for topical use that do not mention the effect claimed by present application, namely, photoprotective activity (photodamage). Together or separately, the mentioned documents do not compromise the non-obviousness of the present invention.

None of the references mentions the main subject-matter of the present application, which refers to the incorporation of the extract of *Pothomorphe* in a gel formulation, with the specified components and with photoprotective activity and other effects as claimed in claim 28. In order to obtain these effects, it is necessary permeate the skin, which was also an object of the present invention. The Examiner did not properly take into account these properties that characterize the invention.

Further, according to the Examiner, any antioxidant added to any formulation would produce the effect showed in claim 28. Applicants respectfully disagree with the Examiner. Not all photoprotectors are antioxidants. In most cases, the photoprotector acts as a barrier function and has no antioxidant activity. Also, not all antioxidants have photoprotective activity, and in equal intensity. One reason for this is that for performing the effect demonstrated in the present application, the active ingredient must permeate the skin which was only achieved in the present application (Figure 3). The present application was able to dissolve and stabilize the 4-nerodliycathecol, a highly lipophilic molecule, in a totally hydrophilic gel formulation, while at the same time, delivering the active principle into the skin at an adequate rate in sufficient amounts, demonstrating the importance of an appropriate gel composition for an accurate penetration of the drug.

The Examiner says, in the page 6, paragraph 3, that "none of the references, including Uchimyama et al., expressly teach providing the skin therapeutic *Pothomorphe umbellata* extract within a skin gel composition - including one containing carboxymethylcellulose, propylene glycol, and methylparaben, as instantly claimed." Applicants submit that this statement contradicts Examiner's earlier statements.

Based on the above references, it would not have been obvious to imagine an extract of *Pothomorphe* in a gel formulation with the specified components. Furthermore, it would not be possible to foresee that such gel composition with *Pothomorphe umbellata* extract had photoprotective activity. Consequently, Applicants respectfully request that the Board overturn the Examiner's rejections as to claims 24, 27 and 28.

CONCLUSION

In view of the above arguments, Appellant respectfully submits that all the instant claims are allowable over the cited prior art and that the application is in condition for allowance. Accordingly, Appellant respectfully requests the Board of Patent Appeals and Interferences to overturn the rejections set forth in the Final Office Action.

Date: November 12, 2009

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VIII. CLAIMS APPENDIX
(37 C.F.R. 41.37(c)(1)(viii))

1-23. (Canceled)

24. (Previously Presented) A gel composition comprising:

a) carboxymethylcellulose from 0.01 to 2.0%;

b) propylene glycol from 5.0 to 20.0%;

c) methylparaben from 0.1 to 1.0%; and

d) 4-nerolidylcatechol from 0.005 to 20.0%.

25-26. (Canceled)

27. (Previously Presented) A gel composition according to claim 24, wherein said composition is presented for topical use.

28. (Previously Presented) A method of treating skin photodamage, cutaneous aging and/or skin cancer comprising topically administering a gel composition comprising:

a) carboxymethylcellulose from 0.01 to 2.0%;

b) propylene glycol from 5.0 % to 20.0%;

c) methylparaben from 0.1 to 1.0%;

d) 4-nerolidylcatechol from 0.005 to 20.0%;

wherein said gel composition is topically applied to the skin of an animal in need thereof.

29-30. (Canceled)

IX. EVIDENCE APPENDIX

There is no supplemental evidence presented with this appeal.

X. RELATED PROCEEDINGS APPENDIX

There are no proceedings related to this application.